

What is Claimed is:

1. A method for determining the exons present in a potentially variantly spliced mRNA, said method comprising the steps of:

(a) providing a potentially variantly spliced mRNA, said mRNA encoded by a DNA, said DNA comprising a plurality of exons, each of which plurality of exons may or may not be included in said mRNA;

(b) providing an array, said array comprising a plurality of different primers immobilized on a solid support at distinct locations thereon, with each of said plurality of different primers selectively hybridizing to a corresponding one of said plurality of exons to form a duplex therebetween;

(c) contacting said mRNA to said array so that a duplex is formed between each different primer and each corresponding exon if said corresponding exon is included in said mRNA;

(d) subjecting said duplexes to a primer extension reaction so that the primers in said duplexes are extended with at least one labeled base; and then

(e) detecting the presence or absence of said labeled base in each of said plurality of primers, the presence of said at least one labeled base indicating the presence of the exon to which said primer selectively binds in said potentially variantly spliced mRNA.

2. The method according to claim 1, wherein said mRNA comprises mRNA fragments.

3. The method according to claim 1, further comprising the step of fragmenting said mRNA prior to said contacting step.

4. The method according to claim 1, wherein said primer extension reaction is carried out with a reverse transcriptase having a deleted RNase H segment.

5. The method according to claim 1, wherein said primers are immobilized to said solid support by the 5' end thereof so that the 3' ends of said primers are available to be extended in said primer extension reaction.

6. The method of claim 1, wherein said mRNA is provided from a biological sample.

7. The method according to claim 1, wherein said mRNA is produced by polymerization from a corresponding cDNA.

8. The method according to claim 1, wherein said mRNA is CD44 mRNA.

9. A method according to claim 1, wherein said detecting the step is followed by the steps of:

(f) generating a plurality of values, each of said values indicating the presence or absence of each of said exons in said mRNA; and then

(g) generating a code representing the exons present in said mRNA from said plurality of generated values.

10. The method of claim 9, wherein each of said values is a digital value, and said code is a digital code.

11. The method of claim 9, wherein each of said values is a binary value, and said code is a binary code.

12. A method for distinguishing splice variants in a mixed mRNA sample, said method comprising the steps of:

(a) providing a mixed mRNA sample, said mixed mRNA sample comprising a plurality of splice variants, each one of said plurality of splice variants containing a distinct exon-exon junction not found in each other of said plurality of splice variants;

(b) providing an array, said array comprising a plurality of different primers immobilized on a solid support at distinct locations thereon, with each of said plurality of different primers selectively hybridizing to a corresponding one of said distinct exon-exon junctions to form a duplex therebetween;

(c) contacting said mixed mRNA sample to said array so that a duplex is formed between each different primer and each corresponding splice variant if said corresponding splice variant is included in said mixed mRNA sample;

(d) subjecting said duplexes to a primer extension reaction so that the primers in said duplexes are extended with at least one labeled base; and then

(e) detecting the presence or absence of said labeled base in each of said plurality of primers, the presence of said at least one labeled base indicating the presence of the splice variant to which said primer selectively binds in said mixed mRNA sample.

13. The method according to claim 12, wherein said plurality of splice variants comprises at least three splice variants.

14. The method of claim 11, wherein said detecting step (e) is followed by the step of:

(f) determining the presence of at least three distinct splice variants in said sample from said detected presence or absence of said labeled base in each of said plurality of primers.

15. The method according to claim 12, wherein:

a plurality of said splice variants contains an exon-exon junction comprising a common exon segment coupled to a variable exon segment, with said common exon segment being the same among said plurality of splice variants and said variable exon segments being different among said plurality of splice variants;

a plurality of said primers contains a common primer segment coupled to a variable primer segment, with the common primer segment corresponding to said common exon segment and being the same among said plurality of primers, and with said variable primer segment corresponding to said variable exon segment and being different among said plurality of primers; and

said common primer segments are from 8 to 50 nucleotides in length and are positioned at the 5' end of said primers, and said variable primer segments are from 2 to 7 nucleotides in length and are positioned at the 3' end of said primers.

16. The method according to claim 12, wherein said mRNA comprises mRNA fragments.

17. The method according to claim 12, further comprising the step of fragmenting said mRNA prior to said contacting step.

18. The method according to claim 12, wherein said primer extension reaction is carried out with a reverse transcriptase having a deleted RNase H segment.

19. The method according to claim 12, wherein said primers are immobilized to said solid support by the 5' end thereof so that the 3' ends of said primers are available to be extended in said primer extension reaction.

20. The method of claim 12, wherein said mRNA is provided from a biological sample.

21. The method according to claim 12, wherein said mRNA is produced by polymerization from a corresponding cDNA.

22. The method according to claim 12, wherein said mRNA is CD44 mRNA.

23. A method according to claim 12, wherein said detecting the step is followed by the steps of:

(f) generating a plurality of values, each of said values indicating the presence or absence of each of said exons in said mRNA; and then

(g) generating a code representing the exons present in said mRNA from said plurality of generated values.

24. The method of claim 23, wherein each of said values is a digital value, and said code is a digital code.

25. The method of claim 23, wherein each of said values is a binary value, and said code is a binary code.

26. An array useful for determining the exons present in a potentially variantly spliced mRNA, said mRNA encoded by a DNA, said DNA comprising a plurality of exons, each of which plurality of exons may or may not be included in said mRNA, said array comprising:

a solid support; and

a plurality of different primers immobilized on said solid support at distinct locations thereon, with each of said plurality of different primers selectively hybridizing to a corresponding one of said plurality of exons under predetermined hybridization conditions;

wherein said primers are immobilized to said solid support by the 5' end thereof;

and wherein said mRNA is CD44 mRNA.

27. An array according to claim 26, wherein said plurality of primers comprise at least three primers.

28. An array according to claim 26, wherein each of said plurality of primers is from 10 to 50 nucleotides in length.

29. An array useful for distinguishing splice variants in a mixed mRNA sample, said mixed mRNA sample comprising a plurality of splice variants, each one of said plurality of splice variants containing a distinct exon-exon junction, each of said distinct exon-exon junctions comprising a common exon segment coupled to a variable exon segment, with said common exon segment being the same among said plurality of splice variants and said variable exon segments being different among said plurality of splice variants, said array comprising:

a solid support; and

a plurality of different primers immobilized on said solid support at distinct locations thereon, with each of said plurality of different primers selectively

hybridizing to a corresponding one of said distinct exon-exon junctions under predetermined hybridization conditions to form a duplex therebetween;

wherein each of said plurality of primers contains a common primer segment coupled to a variable primer segment, with said common primer segment corresponding to said common exon segment and being the same among said plurality of primers, and with said variable primer segment corresponding to said variable exon segment and being different among said plurality of primers;

and wherein said common primer segments are from 8 to 50 nucleotides in length and are positioned at the 5' end of said primers, and said variable primer segments are from 2 to 7 nucleotides in length and are positioned at the 3' end of said primers.

30. An array according to claim 29, wherein said plurality of primers comprise at least three primers.

31. A system for determining the exons present in a potentially variantly spliced mRNA with a plurality of different primers, each of said plurality of primers selectively hybridizing to a corresponding one of said plurality of exons, and each of said plurality of primers being extended with at least one labeled base when said corresponding one of said plurality of exons is present, said system comprising:

(a) a detector for detecting the presence or absence of said labeled base from each of said plurality of primers;

(b) a signal generator operatively associated with said detector for generating a plurality of values, each of said values indicating the presence or absence of each of said exons in said mRNA from said detected presence or absence of said labeled base from each of said plurality of primers; and

(c) a processor operatively associated with said signal generator for generating a code representing the exons present in said mRNA from said plurality of generated values.

32. A system according to claim 32, further comprising a storage device operatively associated with said processor for storing said code.

33. A system according to claim 32, further comprising a display operatively associated with said processor for displaying said code.

34. A system according to claim 32, wherein each of said values is a digital value, and said code is a digital code.

35. A system according to claim 32, wherein each of said values is a binary value, and said code is a binary code.

36. A system for distinguishing splice variants in a mixed mRNA sample with a plurality of different primers, each of said plurality of primers selectively hybridizing to a distinct exon-exon junction in each of said plurality of splice variants, and each of said plurality of primers being extended with at least one labeled base when said corresponding one of said plurality of exons is present, said system comprising:

(a) a detector for detecting the presence or absence of said labeled base from each of said plurality of primers;

(b) a signal generator operatively associated with said detector for generating a plurality of values, each of said values indicating the presence or absence of each of said splice variants in said mixed mRNA sample from said detected presence or absence of said labeled base from each of said plurality of primers; and

(c) a processor operatively associated with said signal generator for generating a determination of the splice variants present in said mixed mRNA sample from said plurality of generated values.

37. A system according to claim 36, further comprising a storage device operatively associated with said processor for storing said determination of the splice variants present in said mixed mRNA sample.

38. A system according to claim 36, further comprising a display operatively associated with said processor for displaying said determination of the splice variants present in said mixed mRNA sample.

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